REMARKS

I. Support for the Amendments

Claims 1-32 were originally in the application. Claims 1-25 and 38 have been canceled, and claims 29-32 have been withdrawn. Claims 26-27, 33-37, and 39-44 were previously in the application.

Claims 26-27, 33-37, and 39-44 are currently in the application. Claims 26-27, 33-37, 39, 43, and 45 have been amended.

Support for amended claims 26-27, 33-37, 39, 43, and 45 can be found in the original specification, figures, and claims. Support for these amendments can also be found in the previous versions of these claims. No new matter has been added by virtue of these amendments.

Additional support for amended claims 26-27, 33-37, 39, 43, and 45 can be found, e.g., from page 1, line 29, to page 2, line 4; from page 2, line 11, to page 3, line 5; and in the Examples and Figures. Additional support for amended claims 26-27, 43, and 45 can be found, e.g., in the Abstract; on page 1, lines 17-18; on page 6, line 31; from page 6, line 27, to page 9, line 27; in Tables 1-3; and in the Examples.

II. Status of the Claims

Claims 1-32 were originally in the application. Claims 1-25 have been cancelled. Claims 26-32, which were previously non-elected claims in U.S.S.N. 09/354,664, were previously in the application. Claims 26-32 were subject to a restriction requirement. Claims 26-28 were elected.

In the previous amendment, claims 26 and 39 were amended, and claim 38 was canceled.

Claims 26-27, 33-37, and 39-44 are currently in the application. Claims 26-27, 33-37, 39, 43, and 45 have been amended.

III. Reiteration of the Request for a Corrected Filing Receipt

On 14 November 2003, Applicants filed a Request for Corrected Filing Receipt, but did not receive it. Applicants continue to await a revised, corrected filing receipt, as noted in the reminder requests in the Amendments filed on 28 November 2006, 13 July 2007 (copy also provided with Request for Continued Examination on 12 October 2007), and 9 May 2008.

Applicants hereby reiterate their request to receive the Corrected Filing Receipt forthwith.

IV. The Rejection of Claims 26-27, 33-34, 37, 39, and 41-42 under 35 U.S.C. §102(b) is Traversed in Part and Accommodated in Part

The Examiner has rejected claims 26-27, 33-34, 37, 39, and 41-42 under 35 U.S.C. § 102(b) for alleged anticipation by Fujishiro (JP 07-250681). Applicants respectfully traverse this rejection, but have amended claim 26 to further prosecution in a timely manner.

Claim 26 has been amended to emphasize that the dry matrix or solid medium comprises i) a weak base; ii) a chelating agent; and iii) an anionic surfactant or an anionic detergent.

In addition, Applicants respectfully submit that Fujishiro does not anticipate the claims to the present invention. For example, Fujishiro describes the use of a cartridge system first to trap

bacteria and then to bind the DNA on a glass fiber filter. Once the bacteria are trapped, an external bacterial cell lysis solution containing an RNase is added to liberate the DNA so it can then bind to the glass fiber matrix.

In contrast, in the presently claimed invention, there is no plurality of filters in series, and the lysis agents are incorporated into the matrix so that DNA binds in a non-chemical manner.

In addition, as Dr. Walter King, Vice President of Research & Development of Whatman PLC, stated in his Declaration (submitted concurrently herewith), **Fujishiro is directed to a sequential method of plasmid purification** that not only calls for the **removal of RNA** (see, e.g., [0011]), but also for **sequential movement (and purification of the plasmid DNA) into a second cartridge**, this one **containing glass in fiber or powder form** (see, e.g., [0020]-[0025]). Fujishiro **neither describes nor suggests sorbing the lysing agents to yield a dry matrix or solid medium**. Moreover, Fujishiro **teaches away from such a matrix or medium** by the fact that Fujishiro identifies sequential processing steps of lysis, digestion of RNA, and transport to a DNA binding medium, which can only mean that Fujishiro **never envisioned that all steps could be embodied on a single surface with less processing**. Instead, Fujishiro **emphasizes the need for sequential use of separate cartridges**.

He also points out that in the "Means for Solving the Problem" (see [0005]), **Fujishiro describes a process having a *first* cartridge for bacteriolysis and a decomposition process for RNA, *followed by* adsorption of DNA, washes, and elution in a *second* cartridge. Fujishiro states that "[p]lasmid DNA is mainly adsorbed by the glass powder layer"** (see [0013], all emphasis added) **in the *second* cartridge**.

As Dr. King also notes, in another example, Fujishiro describes the ***first* cartridge**, which is shown in Drawing 1 (see [0014]-[0019] and Drawing 1). **The Office Action refers specifically to the filter compositions in the *first* cartridge in this portion of the specification.** However, **the trap filter** (1), which may be a glass fiber filter, a polyethylene resin filter, a non-woven fabric filter, or other material, **is the layer used for uptake of the**

"fungus bodies" resulting from bacteriolysis – not for the isolation of the plasmid DNA (see [0016], all emphasis added). Moreover, **the membrane filter** (2), which may be cellulose acetate, polyvinylidene fluoride, or other material, is **"mainly a layer for filtration and removal of discard, such as coagulation protein and Chromosome DNA"** – again not for the isolation of the plasmid DNA (see [0017], all emphasis added). Rather, **the isolation of plasmid DNA takes place in the *second* cartridge**, which is shown in Drawing 2 (see [0020]-0025] and Drawing 2), where "**[t]he glass powder layer 22 is mainly a layer for DNA adsorption**" (see [0022], all emphasis added). This layer is prepared from a glass powder suspension and is sandwiched between **two glass fiber filters** (21, 23), which "**are mainly the layers for plasmid adsorption *assistance***" (see [0020]-[0022], [0024] and Drawing 2, all emphasis added).

In essence, the sample encounters a series of filters in the first and second cartridges with the *isolation of the plasmid DNA* taking place on the *glass powder layer* in the *second* cartridge. Fujishiro **never envisioned that all steps could be embodied on a single surface with less processing**. Instead, Fujishiro **emphasizes the need for sequential use of separate cartridges**. Therefore, the disclosure of **Fujishiro does not anticipate the present invention and even teaches away from the present invention**.

In view of the foregoing, Applicants respectfully submit that claims 26-27, 33-34, 37, 39, and 41-42 fulfill the requirements of 35 U.S.C. §102(b), and request the Examiner's reconsideration of these claims accordingly.

V. The Rejection of Claims 26-27, 33-37, and 39-48 under 35 U.S.C. §103(a) is Traversed in Part and Accommodated in Part

The Examiner has rejected claims 26-27, 33-37, and 39-48 under 35 U.S.C. § 103(a), alleging obviousness over Rogers et al. (Analyt. Biochem. 247: 223-227 [May 1997]; "Rogers & Burgoyne" or "Rogers") in view of Burgoyne (U.S. Patent 5,496,562) and in view of Kahn et al. (Methods Enzymol. 68: 268-280 [1979]; "Kahn"). Applicants respectfully traverse this rejection.

The Patent Office alleges that Rogers shows recovery of DNA from bacterial liquid cultures by application of the culture to the FTA® solid medium, followed by PCR. The Patent Office concedes that Rogers does not show use of bacteria comprising vectors or media comprising micromesh plastic and that Rogers does not detail the composition of the chemicals in the FTA® medium, but references the Burgoyne patent. The Patent Office then focuses on columns 2-4 and Example 2 (cols. 4-6) of Burgoyne with respect to disclosure of the cellulose or plastic micromesh solid support, the chemical composition, and the application and storage of isolated pUC19 plasmids, followed by their recovery. Finally, the Patent Office notes that claim 6 claims application and recovery of generic DNA. The Patent Office cites Kahn for replication of vectors in bacterial and for the usefulness of the vectors.

Applicants have already discussed these references at length. For the reasons already on record, Applicants respectfully traverse this rejection.

Applicants note that Rogers & Burgoyne describes experiments with genomic DNA. Kahn mentions how plasmid DNA can be separated from genomic DNA on the basis of its smaller size or its unique properties of it being a covalently closed circular DNA or, in other words, less complex than genomic DNA, but this reference actually teaches away from the present invention. For example, as Applicants have previously noted, plasmid DNA behaves differently from genomic DNA based on its composition and its structure. It would not be expected that less complex DNA would interact with a solid matrix in the same manner as genomic DNA, so it would not be intuitive that plasmid DNA could be isolated on a solid matrix.

As Applicants noted previously, Burgoyne speaks of using purified plasmid DNA as an experimental source of double stranded DNA in order to show that purified DNA on FTA® is stable when followed by plastic coating. In contrast to the present invention, Burgoyne does not disclose vector DNA isolated directly from cells, however. Rather, in Burgoyne, the plasmid DNA was first purified by state of the art methods at the time, then applied to FTA®. It is not

intuitive that adding the cells directly would have purified the plasmid DNA. Burgoyne only demonstrates DNA isolation directly from cells for genomic DNA.

In a previous Amendment, Applicants pointed out that it could not have been assumed that plasmid DNA would elute from bacterial cultures on FTA® medium in the same manner as chromosomal DNA, citing, e.g., Old & Primrose as two examples of the different properties of chromosomal DNA and plasmid DNA. Applicants respectfully submit that, while this present invention does not relate either to density in the presence of ethidium bromide, or to denaturation at pH 12.0-12.5, the reference nevertheless underscores the fact that **differences in the properties** of chromosomal DNA and plasmid DNA demonstrate the **lack of predictability** that a method that works with one type of DNA will work with the other.

As the following argument was new to the previous Amendment (but was not addressed by the Patent Office in the present Office Action), Applicants respectfully draw the Examiner's attention to the Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc., Fed. Reg. 72(195): 57526-57535 (Oct. 10, 2007). The teaching/suggestion/motivation test **is** listed as Rationale G on page 57529. (For the reasons discussed above and in previous Amendments, the present invention is not predictable under Rationales A-E, and Rationale F is inapplicable to the present situation.)

In addition, as Dr. Walter King, Vice President of Research & Development of Whatman PLC, stated in his Declaration (submitted concurrently herewith), Rogers shows recovery of DNA from bacterial liquid cultures by application of the culture to the FTA® solid medium, followed by polymerase chain reaction (PCR) amplification of **genomic** DNA ***in situ* on FTA® medium**. Rogers tests only **bacterial strains**. The sequence that Rogers amplifies, and hence detects, is **not a vector** component (and hence **not a plasmid**), but rather the ribosomal RNA genes of the **chromosomal/genomic DNA** (see p. 224, col. 2, "PCR Primers"). Rogers does not show use of bacteria comprising vectors or media comprising micromesh plastic, and Rogers does not detail the composition of the chemicals in the FTA® medium, but references the

Burgoyne patent. Moreover, there is no suggestion in Rogers that the cells in the samples contain both genomic DNA and plasmid DNA mixed together. Rogers does **not** demonstrate **plasmid** DNA isolation on a solid medium or matrix **directly from cells containing a mixture of both genomic DNA and plasmid DNA**.

As Dr. King points out, although the Rogers paper references the Burgoyne patent, the Rogers paper and the Burgoyne patent, taken either alone or together, neither disclose nor suggest the present invention. The deficiencies of Rogers are **not** remedied by the disclosure of Burgoyne. Burgoyne describes a solid matrix having a compound or composition comprising uric acid, together with a weak base. Burgoyne alternatively describes a composition comprising a monovalent weak base (such as Tris), a chelating agent (such as EDTA), an anionic detergent (such as SDS), and optionally uric acid or a urate salt sorbed to a cellulose-based paper. In Example 2, Burgoyne describes the application of **previously purified** plasmid pUC19 (i.e., purified from cellular components **and purified from genomic DNA**), whereby the **previously purified** plasmid pUC19 in solution in TE buffer is dried onto Whatman No. 1 paper, which has been soaked with a solution of 40 ml mM uric acid and 100 mM Tris (free base), and then is then sheathed in protective polystyrene and later chloroform extracted to remove the protective layers (Example 2.5; col. 5, l. 54, to col. 6, l. 21). In contrast to the present invention, **Burgoyne does not disclose plasmid vector DNA** isolated **directly from cells**, however. Rather, in Burgoyne, the plasmid DNA is first purified by state of the art methods at the time then applied to the treated matrix. According to Dr. King, it is **not** intuitive that adding the cells directly would have purified the plasmid DNA. The **only** time Burgoyne demonstrates DNA isolation directly from cells is for **isolation of genomic DNA** (Examples 1 and 3). As with Rogers, Burgoyne does **not** demonstrate **plasmid** DNA isolation on a solid medium or matrix **directly from cells containing a mixture of both genomic DNA and plasmid DNA**.

Further, Dr. King points out that the deficiencies of the Rogers paper and the Burgoyne patent are **not** remedied by the disclosure of the Kahn paper. Kahn describes the use of bacterial plasmid as vehicles for the stable maintenance of foreign DNA in bacteria (p. 268). Kahn reviews various plasmid cloning vectors. However, **Kahn teaches away from the present invention, as well as the Rogers paper and the Burgoyne patent,** by emphasizing that the

different properties of plasmid DNA and chromosomal genomic DNA can be used to separate these two types of DNA. For example, Kahn states that "**[p]lasmid DNA can be separated from chromosomal DNA on the basis of its smaller size or** by taking advantage of **the unique properties of covalently closed circular DNA molecules**" (p. 269; all emphasis added). Among the methods Kahn describes as taking advantage of these distinctive properties are cesium chloride (CsCl)-ethidium bromide (EtBr) gradient centrifugation, pH adjustment, separation using acid phenol and low salt, and methods using polyethylene glycol (PEG) or hydroxyapatite (pp. 269-271). **These methods underscore the distinctive properties of plasmid DNA vs. chromosomal/genomic DNA and the need for multi-step liquid purification, even for the smaller samples.** As with Rogers and Burgoyne, Kahn does **not** demonstrate **plasmid** DNA isolation on a solid medium or matrix **directly from cells containing a mixture of both genomic DNA and plasmid DNA**.

As Dr. King states, the teachings of Rogers, Burgoyne, and Kahn, either alone or in combination, do not suggest the present invention. If anything, taken together, these references emphasize the need to isolate either genomic DNA without plasmids (Rogers) or previously purified plasmid DNA (i.e., without genomic DNA in the sample) (Burgoyne) and the differences in the properties of the two types of DNA (Kahn).

As Dr. King notes, the present invention specifically mentions the use of plasmids as the vectors (see, e.g., the Abstract; p. 1, ll. 17-18; p. 6, l. 31; Tables 1, 2 and 3 of Example 1, and Examples 2 and 3) and the isolation of plasmids directly from a host cell without previous removal/purification from chromosomal/genomic DNA. The possibility of directly isolating plasmids from a host cell or virus in accordance with the present invention was not obvious from Rogers, and indeed, Burgoyne, both of which, either alone or together, teach away from the invention by working only with genomic DNA without plasmids or with previously purified DNA (see, e.g., the references to the Burgoyne patent at page 3 (ll. 4-5) and, in particular, from page 14 (l. 18) to page 15 (l. 4), while Kahn only emphasizes the distinctive properties of the two types of DNA.

Plasmids are structurally and size-wise different from genomic DNA in that they are much smaller and circular (often supertwisted/supercoiled DNA). While the results of the Rogers paper show that genomic high molecular weight DNA does remain on the FTA® paper following washing, Rogers does not show that such a procedure could result in adequate recovery of plasmid DNA for use in transformation assays. Clearly, Rogers does not use bacterial strains containing these lower molecular weight plasmid structures and as such could not demonstrate that such plasmid DNAs could be recovered as detected by PCR. The present invention shows that plasmid DNA is found in the TE buffer washes (see, e.g., p. 15, ll. 6-22). Thus, Dr. King additionally maintains that the present invention provides a method where the normally discarded wash solution from FTA® contains the biologically active transforming plasmid DNA. The present application demonstrates the ability of **plasmid** DNA to **elute** from the washed punch after a 20-minute incubation in buffer at room temperature such that the **plasmid vector** DNA is **isolated *from* the FTA® medium** (e.g., p. 13, ll. 3-6). In the present application, two different **host *cells***, bacteria and yeast, each containing plasmid DNA were applied to FTA® cards. The specification shows that the **cells** were lysed and the **plasmid** DNA retained and protected by the FTA® chemicals during room temperature storage (for at least 3 months; p. 18, ll. 28-29). **M13 plaques and cells** infected with **M13 bacteriophage** were also used (see Example 4). As shown in Examples 1-2, ***plasmid* DNA *directly from host cells* can be *eluted by washing* in order to isolate it *from* the FTA® card** (see, e.g., p. 17, ll. 1-17 and Table 4; p. 13, ll. 3-6; p. 14, ll. 16-18 and 25-30).

As discussed both previously and in Dr. King's Declaration, **plasmid DNA behaves differently from genomic DNA based on its composition and its structure. It would *not* be expected that less complex DNA would interact with a solid matrix in the same manner as genomic DNA, so it would *not* be intuitive that plasmid DNA could be isolated on a solid matrix.**

Genomic DNA, due to its large size relative to plasmid DNA, behaves differently under various circumstances. **Differences in the properties of genomic vs. plasmid DNA have been exploited in a wide range of laboratory processes**, e.g., in DNA isolation in order to separate

the two types of DNA. Examples of references demonstrating and/or exploiting the different properties of these two types of DNA include Hansen & Blakesley, "Simple Archiving of Bacterial and Plasmid DNAs for Future Use," Focus 20(3): 72-74 (1998), and Old & Primrose, Principles of Gene Manipulation (4th ed.), Blackwell Scientific Publications (Boston: 1989), copies of which have been previously provided to the Examiner. These references are discussed at length in Dr. King's Declaration. The fact that these protocols are, not surprisingly, different than the protocols of the present invention does not render them irrelevant. Rather, these references serve to underscore the fact that ***differences in the properties*** of chromosomal DNA and plasmid DNA demonstrate the ***lack of predictability*** that a method that works with one type of DNA will work with the other and have been brought to the attention of the Patent Office as evidence of the inherently different properties of the two types of DNA and to show that the combination of the Rogers, Burgoyne, and Kahn references, which relate to disparate subject matter, would not be obvious. Moreover, as with Old & Primrose and Hansen, Kahn emphasizes the distinctive properties of the two types of DNA.

In view of the foregoing, Applicants respectfully submit that remaining claims 26-27, 33-37, and 39-48 fulfill the requirements of 35 U.S.C. §103(a), and request the Examiner's reconsideration of these claims accordingly.

CONCLUSION

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

Applicants hereby request a three-month extension of time for the Amendment and accompanying materials. If, however, a petition for an additional extension of time is required, then the Examiner is requested to treat this as a conditional petition for an extension of time and the Commissioner is hereby authorized to charge our deposit account no. 04-1105 for the appropriate fee. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

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